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Dear Josh,

I am writing to ask your advice on symbols for the characters of vaccinia virus. I think that we have now reached the stage where a proper genetic study of this virus is possible, though still laborious and inaccurate when compared with phage. It is important that terminology should be straightened out now, for the retention of a lab jargon such as Burnet uses for flu makes comprehension of papers difficult (as I know as a reader of his papers!).

The position at present is that with two different strains of virus we have unequivocal evidence of recombination affecting a number of different characters (Virology 1958, 5, No. 3, 530). Since then I have obtained a similar range of recombinants from single mixedly infected cells, isolated in microdrops. The weakness of this approach was that the two parental types differed in a whole range of unknown markers as well as those we looked at. We now have a way out of this by using the "white variants" of strains which produce red pocks on the chorioallantoic membrane. Study of a number of white variants of rabbitpox shows that they are genetically different (they differ in other characters than "whiteness", and they recombine with high frequency to produce wild type). Thus we should, during the coming year, be able to press on with our study of the genetic structure of vaccinia virus (to which "rabbitpox" belongs) using different mutants of one parental strain.

The characters with which we have so far been concerned, and my suggested symbols for them, are as follows:-

(1) Pock character on the chorioallantoic membrane.

A complex character involving the response of the chick embryo as well as the multiplication characteristics of the virus. The broad division is into "red" and "white" pocks.

My suggestion is w (for "white")

w^+ is the "red" wild type

w_1 to w_n are "white" mutants, of which there are a great number.

An alternative, which may be preferable, would be to equate "red" with "ulcer" and "white" with "non-ulcerated lesion".

We would have u^+ = wild type (ulcerated lesion)

u_1 to u_n = "white" mutants, non ulcerating.

The advantage is that one doesn't use a contradictory symbol like w^+ for a red pock; but u^+ for ulcerated and u for non-ulcerated.

(2) Plaque character on chick embryo fibroblasts.

Wild type (w^+) strains produce large plaques. Various w mutants produce smaller plaques, or plaques with irregular edges, or plaques the same size as w^+. I suppose the appropriate abbreviation would be similar to that used by phage geneticists:

i.e. "m" "fu" for fuzzy, etc.

(One difficulty here is that certain white mutants produce minute plaques, i.e. they are probably two expressions of one mutation.)

(3) Haemagglutinin production.

Sometimes this antigen is not produced:

a^+ = wild type; haemagglutinin produced (a = agglutinin).

a = mutant which fails to produce haemagglutinin.

There may be quantitative differences amongst the "a^+" if measured under standard conditions relative to number of infectious particles, or total particles. (The vaccinia HA is separable from the virus particle.)

(4) Heat Resistance.

t^+ = wild type - temperature resistant (i.e. under standard conditions drops about 1 log in 40' at 55°C)

t = temperature sensitive variant (drops 4-5 logs in 40' at 55°C).

Among some 200 recombinants I haven't yet found any intermediates.

(5) Virulence characters.

In intact animals these are obviously complex and under polygenic control. I do not propose to use them in the early stages of work on the genetics of vaccinia, but these will ultimately be important. In addition we have to consider ability to multiply (or produce plaques) in various types of cell.

These are essentially host range characters, so might be grouped as "h" characters.

Mouse virulence would then be:

hm = high virulence from the mouse (after I-C injection)

hm^-_1 to hm^-_n = virulence from the mouse varying from hm.

(There are several levels of virulence but only extremes can be handled.)

Rabbit virulence would be:

hr = high virulence (large lesion) ~~from~~ in the rabbit, after intradermal injection.

hr^-_1 to hr^-_n = varying lower levels of virulence.

For current work I need to group mouse and rabbit virulence as high, low (-), and intermediate (i), though I am aware that there are quite a number of different "intermediates"; i.e. I would only use the expressions:

hm, hm^- and hm^i

hr, hr^- and hr^i.

For cell lines:

hL^+, hL^- ability to produce plaques on "L" cells

hKB^+, hKB^- ability to produce plaques on KB cells

hCF^+, hCF^- ability to produce plaques on chick fibroblasts.

hH^+, hH^- ability to produce plaques on HeLa cells.

Depending upon how completely a strain has been characterized, and what characters are relevant, the virulence characters might be grouped thus:

h (m r^i L^+ KB^+ CF^- H-).

As we go along, of course, other characters will crop up. What I am concerned with is to get started with reasonable expressions - once that has been done it should not be too difficult to keep it up.

I hope you enjoy your new venture at Stanford.

With best wishes.

Yours sincerely,

Frank Fenner.